APPENDIX A to PSC RESPONSE IN OPPOSITION TO SSC DEFENDANTS' MOTION FOR SUMMARY JUDGMENT

I. Compounding Pharmacies Are Generally Not Regulated by the FDA.

According to the FDA, traditional compounding is the extemporaneous combining, mixing, or altering of ingredients by a pharmacist in response to a physician's prescription. Compounded drugs are mixed in response to a physician's prescription in order to create a medication tailored to the specialized needs of an individual patient.[1] Traditional compounding is used typically to prepare medications that are not available commercially, such as a drug for a patient who is allergic to an ingredient in a mass-produced product, or diluted dosages for children.[2][3] Because the law requires that compounding pharmacies compound specific medications in response to individual prescriptions, compounding pharmacies should not produce medications in bulk for mass distribution.[4] Accordingly, the FDA did not regulate compounding pharmacies to the same degree as pharmaceutical companies.[5] The FDA generally leaves regulation of compounding pharmacies to state pharmacy boards.[6]

II. The Risks of Pharmacy Compounding Were Known Before the Fungal Meningitis Catastrophe

[1] PSOF Nos. 3 and 4.
[2] PSOF No. 5.
[3] Rather than repeat arguments from their prior briefing, Plaintiffs incorporate here the arguments presented in opposition to summary judgment of Plaintiffs' PLA claims against the Saint Thomas Defendants. *See* PSC Mem. Supporting Mot. for Partial Sum. J. [Dkt. 2302], PSC Reply and Opp. [Dkt. 2508], PSC Mem. Supporting Mot. for Reconsideration [Dkt. 2749-1].
[4] PSOF No. 6.
[5] PSOF No. 7.
[6] PSOF No. 8.

The serious risks of pharmacy compounding were the subject of considerable public discussion in the pharmacy community and the medical community before the subject meningitis catastrophe. For example:

- In 2002 (ten years before the meningitis catastrophe), the CDC published a report regarding at least two cases of fungal meningitis arising from contaminated medication used in epidural injections. That report concluded: "purchasers of pharmaceuticals should determine if supplies are provided from a compounding pharmacy that . . . follows appropriate measures to ensure that injectable products are free of contamination."[7]

- On March 24, 2005 (seven years before the meningitis catastrophe), *USA Today* published a front page article with the following headline: "*Safety concerns grow over pharmacy-mixed drugs*." That article discussed growing concern over the fact that drugs produced in bulk by compounding pharmacies are not FDA approved and are not subject to the same oversight as drugs produced by pharmaceutical companies.[8]

- In 2006 (six years before the catastrophe), the FDA conducted a survey of compounded drug products. They collected 36 samples from compounding pharmacies across the United States during unannounced visits. Twelve of the 36 samples (33%) failed analytical testing. The FDA survey concluded "*poor quality compounded drugs are a serious public health concern, as improperly compounded products have been linked to grave adverse events, including deaths*."[9]

- In May 2007 (five years before the catastrophe), the FDA published an article titled: "*The Special Risks of Pharmacy Compounding*." That article highlighted numerous adverse events involving compounded products. It also warned of the emergence of large scale compounding operations that were clearly operating outside the bounds of traditional compounding practice."[10]

- In 2010 (two years before the catastrophe), the FDA posted an educational video on YouTube regarding concerns over the quality of compounded drugs.[11]

- On November 5, 2010 (about two years before the catastrophe), the American Society of Anesthesiologists, the American Society of Health-System Pharmacists ("ASHP") and

[7] PSOF No. 9.
[8] PSOF No. 10.
[9] PSOF No. 11.
[10] PSOF No. 12.
[11] PSOF No. 13.

other medical societies published a joint report regarding drug shortages. That report included an article written by the ASHP stating as follows:

> Compounding pharmacies have also pursued the production of drugs that are in short supply. Caution is warranted because preparations from these pharmacies may not meet applicable state or federal standards (e.g., United States Pharmacopeia chapter 797 or FDA labeling requirements). The sources of raw materials used by compounding pharmacies have been questioned, and apparent lapses in quality control have resulted in serious patient injury, including death.
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> . . .
>
> Compounding pharmacies may also present patient risks; several deaths have been associated with improperly sterilized compounded products.[12]

- In May 2012 (a few months before the meningitis catastrophe), the CDC published a report regarding fungal infections arising from medications obtained from a compounding pharmacy. That report advised that "contamination of compounded sterile preparations has caused outbreaks. Since 1990, FDA has learned of approximately 200 adverse events associated with 71 compounded products."[13]

III. NECC Had a Known History of Regulatory Non-Compliance

Before the meningitis catastrophe, NECC had a history of adverse events relating to its operation as a compounding pharmacy. NECC was the subject of multiple complaints to and investigations by the FDA and the Massachusetts Board of Registration in Pharmacy ("MBP").[14] Those complaints and investigations often focused on unsterile conditions at NECC's facilities.[15] For example, the FDA issued a Warning Letter to NECC in 2006.[16] The FDA letter details numerous problems at NECC including the sale of compounded drugs without patient-specific prescriptions.[17] In addition, the FDA's Warning Letter stated that NECC was compounding copies of commercially available drugs, selling misbranded compounded drugs, and

[12] PSOF No. 14.
[13] PSOF No. 15.
[14] PSOF No. 16.
[15] *Id.*
[16] PSOF No. 17.

experiencing problems with storage and sterility.[18] That warning letter was available to the Tennessee Defendants on the FDA's website long before the meningitis catastrophe.

[17] *Id.*
[18] *Id.*